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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/887,496	06/22/2001	Partha S. Banerjee	18025-1014	7707

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EXAMINER	
JIANG, SHAOJIA A	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 07/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/887,496	BANERJEE ET AL.	
	Examiner	Art Unit	
	Shaojia A Jiang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-64,69-83,87-89,93 and 99-121* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-64,69-83,87-89,93 and 99-121* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

In view of the appeal brief filed on April 12, 2004, PROSECUTION IS HEREBY REOPENED. A new ground of rejection(s) set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) request reinstatement of the appeal.

If reinstatement of the appeal is requested, such request must be accompanied by a supplemental appeal brief, but no new amendments, affidavits (37 CFR 1.130, 1.131 or 1.132) or other evidence are permitted. See 37 CFR 1.193(b)(2).

Currently, claims 1-64, 69-83, 87-89, 93 and 99-121 are pending in this application.

Claims 65-68,84-86, 90-92, and 94-98 are cancelled.

Claims 1-64, 69-83, 87-89, 93 and 99-121 are examined on the merits herein.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-64, 69-83, 87-89, 93 and 99-121 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation "a subject" renders these claims indefinite. The recitation "a subject" is not clearly defined in the claims or specification. One of ordinary skill in the art could not ascertain and interpret the metes and bounds of the patent protection desired as to what "a subject" would be, for example, that the term " subject " would be a single cell, any biological system, an animal or a human, or any non-biological system. Thus, one of ordinary skill in the art could not interpret encompassed thereby.

The recitation, "a derivative" in these claims render claims indefinite. The recitation, "a derivative" is not clearly defined in the specification. Hence, one of ordinary skill in the art could not ascertain and interpret the metes and bounds of the patent protection desired as to "a derivative" of compounds herein, since one of ordinary skill in the art would clearly recognize that many various groups could possibly substituting these compounds. As a result, any significant structural variation to a compound would be reasonably expected to alter its properties, e.g., physical, chemical, physiological effects and functions. Thus, it is unclear as to what "a derivative" of compounds herein would be encompassed thereby.

Claims 11 and 28 contain the trademark/trade names “Britton-Robinson” and “Prideaux-Ward”. Where a trademark or trade or abbreviation name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte*

Simpson, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the abbreviation or trademark or trade name cannot be used properly to identify any particular material or product. A abbreviation or trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a abbreviation or trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name or abbreviation is used to identify/describe particular agent, accordingly, the identification/description is indefinite.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 87-89 are rejected under 35 U.S.C. 112, first paragraph, for scope of enablement because the specification, while being enabling for the treatment or amelioration of diseases or disorders associated with undesired and/or uncontrolled bronchoconstriction disclosed in the specification employing the combination herein, does not reasonably provide enablement for the **prevention** of one or more symptoms of diseases or disorders associated with undesired and/or uncontrolled bronchoconstriction recited in these claims.

The instant claims are drawn to an article of manufacture for the **prevention** of one or more symptoms of diseases or disorders associated with undesired and/or uncontrolled bronchoconstriction. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention: The instant invention pertains to an article of manufacture for the prevention of one or more symptoms of diseases or disorders associated with undesired and/or uncontrolled bronchoconstriction in a human or animal.

The state of the prior art: The skilled artisan would view that the prevention of one or more symptoms of diseases or disorders associated with undesired and/or uncontrolled bronchoconstriction in a human or animal totally, absolutely, or permanently, is highly unlikely, not even occurring at the first time.

The relative skill of those in the art: The relative skill of those in the art is high.

The predictability or lack thereof in the art: The skilled artisan would view that the treatment to prevent one or more symptoms of diseases or disorders associated with undesired and/or uncontrolled bronchoconstriction in a human or animal totally, absolutely, or permanently is highly unpredictable, and not even occur at the first time is highly **unpredictable**.

The amount of direction or guidance presented and the presence or absence of working examples: In the instant case, **no** working examples are presented in the specification as filed showing how to prevent one or more symptoms of diseases or disorders associated with undesired and/or uncontrolled bronchoconstriction in a human or animal totally, absolutely, or permanently, not even occurring at the first time. Note that lack of a working example, is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP 2164. Note that Applicant also admits that bronchoconstriction in a human or animal is "uncontrolled".

Genentech, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the *Wands* factors, e.g., the amount of direction or guidance provided, absence of working examples, and the predictability of the art discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in *undue experimentation* to test the combination in the instant claims whether preventing one or more symptoms of diseases or disorders associated with undesired

and/or uncontrolled bronchoconstriction in a human or animal totally, absolutely, or permanently, with no assurance of success.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-64, 69-83, 87-89, 99-112 and 117-119 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carling et al. (US 5674860, PTO-892) in view of Hochrainner et al. (US 6150418, of record).

Carling et al. discloses a pharmaceutical composition comprising formoterol (free base) or formoterol fumarate salt in combination with the specific steroid anti-inflammatory agent, budesonide, in a pharmaceutically acceptable fluid such as a liquid (see col.4 line 2), by inhalation from a nebulizer (see col.3 line 51) for the treatment of respiratory disorders such as asthma (see title and abstract, col.1 lines 10-15, 46-67). Carling et al. also discloses the effective amount of formoterol, 6-100 μg, preferred 6-48 μg (the instant claimed amount within the range of Carling et al.) in a pharmaceutical composition therein (see col.3 lines 44-45). Carling et al. also discloses that a pharmaceutical composition of the combination therein is formulated into a single dosage administration (see Example 1-3 at col.4). Carling et al. also discloses a kit or

an article of manufacture comprising the same combination and a nebulizer (see col.3 line 8-10 and 50-52, claims 1-36). Carling et al. also discloses the employment of a tonicity adjusting agent herein such as salts of inorganic or organic salts, e.g., succinate, lactate (see col.3 lines 30-38) and adding oleic acid may improve the physical stability (see col.4 line 12-14).

Carling et al. does not expressly disclose the pharmaceutical composition comprising water, a polar solvent or a protic solvent, and buffer providing particular pH value, and the ionic strength of the composition.

Hochrainner et al. discloses a pharmaceutical composition comprising formoterol suitable for storage, in aqueous ethanol of water and ethanol mixture (water and ethanol are well known polar and protic solvents, see col.2 lines 24-34), in the form of a solution or suspension for use in inhalers for nasal therapy, see abstract and claims 1-4 in particular. Hochrainer et al. (6,150,418) further teaches that the pharmaceutical composition is such that it can be administered by inhalation using a suitable nebuliser, see col.4, lines 19-20 and col. 5, lines 33-41. Hochrainer et al. (6,150,418) further teaches that the pH range (preferably between 2.0-7.0 and most preferably between 4.5-5.5), the employment of inorganic acids such as phosphoric acids the employment of buffers in its composition, see in particular col.3, lines 35-40 and col.4 line 55 to col. 5, line 7; and adding inorganic and organic salts (see col.2 lines 56-64),. Hochrainer et al. (6,150,418) finally teaches that additional active ingredients such as steroids could be incorporated in its composition, see claim 19.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ water, a polar solvent or a protic solvent such as ethanol, and to adjust particular pH value by buffer, and to adjust the ionic strength of the composition by adding those inorganic and organic salts taught by Hochrainner et al. and Carling et al.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ water and ethanol and buffer solution in a inhalation composition, since water and ethanol and buffer solution are known to be used in the inhalation composition of Hochrainner et al. comprising formoterol for the same inhalation therapy as Carling et al.

Thus, employing water, ethanol and buffer solution, and adjusting particular pH value by buffer, and adjusting the ionic strength of the composition by adding those inorganic and organic salts taught by Hochrainner et al. and Carling et al. are all deemed obvious since they are all within the knowledge and conventional skills in pharmaceutical science, involving merely routine skill in the art. It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

Claims 1-64, 69-83, 87-89, 99-112 and 117-119 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blondino et al. (US 6004537, PTO-892) in view of Hochrainner et al. (US 6150418, of record).

Blondino et al. discloses a pharmaceutical composition comprising formoterol (free base) or formoterol fumarate salt in combination with the specific steroid anti-inflammatory agent, budesonide (see col.2 lines 9-25), in a pharmaceutically acceptable fluid such as a liquid, co-solvents of alcohols such as ethanol or isopropanol (see col.2 line 55-59), by inhalation from a nebulizer for treatment (see title and abstract, claims 1-30). Blondino et al. also discloses the effective amounts of formoterol, in amount 0.01-0.5% by weight in a pharmaceutical composition therein (see claim 1). Blondino et al. also discloses that the composition or formulation therein is stable under elevated temperatures, e.g., 45^0C (see col.2 lines 35-37). Blondino et al. also discloses that a pharmaceutical composition of the combination therein is formulated into a single dosage administration (see Example 1-4 at col.4). Blondino et al. also discloses a kit or an article of manufacture comprising the same combination and a inhaler (see col.3-4, claims 1-30).

Blondino et al. does not expressly disclose the pharmaceutical composition comprising water and buffer providing particular pH value, and the ionic strength of the composition.

Hochrainner et al. discloses a pharmaceutical composition comprising formoterol suitable for storage, in aqueous ethanol of water and ethanol mixture (water and ethanol are well known polar and protic solvents, see col.2 lines 24-34), in the form of a solution or suspension for use in inhalers for nasal therapy, see abstract and claims 1-4 in particular. Hochrainer et al. (6,150,418) further teaches that the pharmaceutical composition is such that it can be administered by inhalation using a suitable nebuliser,

see col.4, lines 19-20 and col. 5, lines 33-41. Hochrainer et al. (6,150,418) further teaches that the pH range (preferably between 2.0-7.0 and most preferably between 4.5-5.5), the employment of inorganic acids such as phosphoric acids the employment of buffers in its composition, see in particular col.3, lines 35-40 and col.4 line 55 to col. 5, line 7; and adding inorganic and organic salts (see col.2 lines 56-64),. Hochrainer et al. (6,150,418) finally teaches that additional active ingredients such as steroids could be incorporated in its composition, see claim 19.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ water, and to adjust particular pH value by buffer, and to adjust the ionic strength of the composition by adding those inorganic and organic salts taught by Hochrainner et al.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ water and ethanol and buffer solution in a inhalation composition, since water and ethanol and buffer solution are known to be used in the inhalation composition of Hochrainner et al. comprising formoterol for the same inhalation therapy as Blondino et al.

Thus, employing water, ethanol and buffer solution, and adjusting particular pH value by buffer, and adjusting the ionic strength of the composition by adding those inorganic and organic salts taught by Hochrainner et al. are all deemed obvious since they are all within the knowledge and conventional skills in pharmaceutical science, involving merely routine skill in the art. It has been held that it is within the skill in the art

to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

Claim 93 is rejected under 35 U.S.C. 103(a) as being unpatentable over Carling et al. (US 5674860) in view of Hochrainner et al. (US 6150418, of record) further in view of PDR at pages 482, 535, 537, 2828 (of record).

The same disclosures of Carling et al. (US 5674860) in view of Hochrainner et al. have been discussed in the 103(a) rejection set forth above.

Carling et al. and Hochrainner et al. do not expressly disclose further adding one or more agent recited in claim 93 herein to the composition of Carling et al. or Hochrainner et al.

PDR teaches that albuterol (beta2-adrenoreceptor agonist), accolate (leukotriene receptor antagonist) and Zyflo (5-lipoxygenase inhibitor) are all known to be effective in treating asthma.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ a third active such as those enumerated immediately above in a combination composition along with formoterol and budesonide.

One of ordinary skill in the art would have been motivated to employ a third active such as those enumerated immediately above in a combination composition along with formoterol and budesonide because all three actives are known to be useful in treating asthma. Combining two agents which are known to be useful to treat asthma

individually into a single composition useful for the very snme purpose is prima facie obvious. See *In re Kerkhoven* 205 USPQ 1069.

Claims 113-116 and 120-121 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carling et al. (US 5674860) in view of Hochrainner et al. (US 6150418, of record) further in view of Hardman et al. (Goodman Gilman 's *The Pharmacological Basis of Therapeutics*,1996, page 665, of record) or Leckie et al (*Novel Therapy* Of COPD, abstract, Jan 2000, of record).

The same disclosures of Carling et al. (US 5674860) in view of Hochrainner et al. have been discussed in the 103(a) rejection set forth above.

Carling et al. and Hochrainner et al. do not expressly disclose further adding an anticholinergic agent such as ipratropium bromide or tiotropium bromide to the composition of Carling et al. or Hochrainner et al.

Hardman et al. teaches that ipratropium bromide is an anticholinergic agent useful in treating asthma.

Leckie et al teaches that tiotropium is a known bronchodilator employed in treatment of asthma.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ a third active such as ipratropium bromide or tiotropium bromide in a combination composition along with formoterol and budesonide.

One of ordinary skill in the art would have been motivated to employ a third active such as ipratropium bromide or tiotropium bromide in a combination composition along with formoterol and budesonide because all three actives are known to be useful

in treating asthma. Combining two agents which are known to be useful to treat asthma individually into a single composition useful for the very snme purpose is prima facie obvious. See *In re Kerkhoven* 205 USPQ 1069.

Applicant's arguments in the Brief of Appeal filed April 12, 2004 with respect to the prior art rejections made under 35 U.S.C. 103(a) of record in the previous Office Action May 20, 2003 have been considered but are moot in view of the new ground(s) of rejection above.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (571)272-0627. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703.872.9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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June 16, 2004

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